HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Los Angeles District
19900 MacArthur Boulevard Suite 300
Irvine, California 92612-2445

Telephone (714) 798-7600

M439N

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

June 26, 1998

WL-37-8

WARNING LETTER

Mr. Yoram Fishman, President
2-2-0 Laboratories
2375 Third Street
Riverside, CA 92507

Dear Mr. Fishman:

During an inspection of your over the counter (OTC) drug manufacturing facility located at 2375 Third Street, Riverside, California, conducted May 21, to June 1, 1998, our investigator documented deviations from Current Good Manufacturing Practice Regulations (cGMPs), Title 21, Code of Federal Regulations (CFR), Parts 210 & 211. These deviations were noted on the Form FDA-483, List of Inspectional Observations, issued to you at the close of the inspection. Such deviations cause OTC drugs manufactured by your facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

Our investigation revealed there is no assurance that the methods used in or the facilities and controls used in manufacture, processing, packing, or holding of your products are in conformance with the GMP requirements as follows:

1. Failure to confirm the identity and strength of active ingredient(s) in each batch of drug product manufactured [21 CFR 211.165]. For example, finished product testing of ultraviolet sunscreen lotions and other OTC drug products does not include identity and strength of active ingredients, only color, odor, appearance, pH, specific gravity, clarity, and viscosity.

2. Failure to establish and control written procedures which describe in-process controls and tests which are necessary to ensure that drug products and in-process materials conform to their specifications [21 CFR 211.110]. For example, failure to validate the manufacturing process to assure uniformity and homogeneity of drug products.

3. Failure to establish and control written procedures for production and process controls to ensure drug products have the identity, strength, quality, and purity they purport to possess [21 CFR 211.100]. For example, there is no documented evidence which provides a high degree of assurance that your deionized water system which is used to produce your OTC drug products will consistently meet its pre-

determined specifications and quality attributes. Additionally, there is no documentation to support maintenance, cleaning, and repair of deionized water system, nor have any alert limits been established for microbial growth.

4. Failure to establish and control written procedures for cleaning of equipment used in the manufacture, processing, packing, or holding of drug products [21 CFR 211.100]. For example, there are no documented studies to assure the effectiveness of cleaning procedures for mixing tanks and filling equipment used in the manufacture of OTC drug products to ensure the removal of drug and cleaning agent residues from equipment.

5. Failure to establish and control written procedures for calibration of laboratory equipment [21 CFR 211.160]. For example, the autoclave used to prepare media has not been validated and maintenance is not routinely performed to assure proper operation. Also, your ovens used to hold stability samples and temperature monitoring thermometers used in your ovens and incubators have not been calibrated.

6. Failure to ensure that employees are capable of performing their assigned functions and are familiar with the Good Manufacturing Practice (GMP) regulations which are commensurate with their intended duties [21 CFR 211.25]. For example, our inspection revealed that no documented evidence of training exists for personnel involved in the manufacture, inspection, testing, and release of OTC drug products.

Our office has concerns about the corrective measures undertaken by your company to eliminate the recurrence of the deficiencies disclosed in an earlier inspection conducted by our office. Because many of the current deficiencies found during our current investigation are similar to earlier deficiencies. Our office plans to conduct a reinspection of your establishment to ensure that corrections have been implemented.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations.

You should take prompt action to correct these deviations. Failure to do so may result in regulatory action without further notice. Such action includes, but is not limited to seizure and/or injunction. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the violations described in this letter, and as listed on the Form FDA-483 (copy enclosed), including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days,

state the reason(s) for the delay and the time frame within which the corrections will be completed.

Your reply should be addressed to:

Dannie E. Rowland
Compliance Officer
U.S. Food and Drug Administration
19900 MacArthur Boulevard, Suite 300
Irvine, California 92612

Sincerely,

Elaine C. Messa
District Director

cc: State Department of Public Health
Environmental Health Services
Attn: Chief, Food and Drug Branch
601 North 7th Street
PO Box 942732
Sacramento, CA 94234-7320